REMARKS

Claims 2-28, 31, 46, and 48-55 are pending. Claims 1, 29, 30, 32-45, and 47 were previously canceled and claim 25 is canceled herein. Claims 2-7, 11, 12, 15, 17, 18, 20-26, 31, 46, 50-52, and 55 are amended. These amendments find support in the specification and the previously submitted claims; thus, no new matter is presented. Specifically, claim 2 has been amended to recite delivery of dsRNA across the blood-brain and blood-retina barrier as supported by the data in Examples 1-5. Claims 3-4 are amended as to a minor matter of form. Claim 5-6 are amended to properly depend from claim 2. Claims 7, 11-12, 15, 17, 18, 20, 21 are amended as to minor matters of form and to provide proper dependency with antecedent basis. Claims 22-26 are amended as to minor matters of form and to provide proper antecedent basis. Claim 31 is amended as to a minor matter of form. Claim 46 is amended to provide proper dependency. Claim 50-52 and 55 are amended as to minor matters of form. All amendments and cancelations are made without prejudice or disclaimer. Applicants reserve the right to present any cancelled or non-elected claim at a later date in continuation, divisional, or C-I-P applications.

Applicant's attorney wishes to thank the Examiners Hill and Li for the grant of interview on July 11th, 2008. During the interview all of the claims were discussed. Although no agreement was reached, it was indicated that prosecution would be facilitated by amending the claims to present methods of delivery across the blood-brain/blood-retina barrier as shown in Examples 1-5 of the specification. Applicants have complied with this suggestion and present the amended claims herein.

Drawings

The drawings are objected to for "being essentially opaque." Applicants note that these panels show points of fluorescence (or lack thereof) in a tissue . It is impossible to show a lack of fluorescence as anything other than a panel that is essentially opaque, e.g. a lack of fluorescence means that there is no light emitted to expose the film or CCD. Given that the opacity is the basis for evaluating the data, and not an artifact, Applicants respectfully request that the objection be withdrawn.

Specification

The specification is objected to for not having a figure legend. Applicants have amended the specification and the drawings to add the legends, thereby obviating the objection.

Claim Objections

Claims 20 and 26 are objected to regarding minor typographical errors. These claims are amended herein, thereby obviating the objection.

Claims 2-13, 19-22, 24-28, 31, 46, and 48-54 are rejected under 35 USC § 112, first paragraph regarding written description. It is alleged that the claims fail to describe the genus of dsRNA molecules that achieve specific inhibition of gene targets in the eye. Without acceding to the rejection, Applicants have amended independent claim 2 (and thereby remaining dependent claims 3-13, 19-22, 24-28, 31, 46, and 48-54) to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. See the specification page 12, lines 1-6. The method is operative irrespective of the intended target gene or purpose that the dsRNA is introduced. By disclosing double stranded oligonucleotides that cross the barrier, it is moot as to what the target sequence is. Further, the description of an operative example of dsRNA crossing the barrier as in Examples 1-5, sufficiently meets the written description requirement for the genus of all dsRNA molecules that can cross the barrier. As such, Applicants respectfully request withdrawal of the rejection.

Claims 2-13, 20-22, 24-28, 31, 46, and 48-49, and 51-54 are rejected under 35 USC § 112, first paragraph as lacking enablement. It is alleged that while the claims to inhibiting eGFP are enabling, a method for inhibiting other genes is not. Without acceding to the rejection, Applicants have amended independent claim 2 (and thereby remaining dependent claims 3-13, 20-22, 24-28, 31, 46, and 48-49) to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. As discussed previously, such a method can be used for any intended target gene or purpose. By disclosing a method for trafficking double stranded oligonucleotides across the barrier, it is moot as to what the target sequence is. Further, it is noted that the Office Action states that the claims are enabled regarding trafficking dsRNA across the

barrier. See, Office Action mailed January 24, 2008, pages 12 and 14. As such, Applicants respectfully request withdrawal of the rejection.

Claims 2-13, 19-22, 24-28, 31, 46, and 48-54 are rejected under 35 USC § 112, second paragraph as being indefinite.

Specifically, claim 2 is objected to for failure to recapitulate the preamble. Applicants have amended claim 2 in accordance, thereby obviating the rejection.

Further, claims 3 and 26 are rejected for reciting "preferably." Applicants have amended claims 3 and 26 to remove the term. Thus, the rejection is obviated.

In addition, claim 8 is alleged to be indefinite for reciting the "inner segment of the eyeball." Applicants respectfully disagree. The specification states that "in an embodiment of the present invention said cells or tissues are cells or tissues of the inner segment of the eye ball, preferably retinal cells, and particularly preferred cells of the retinal pigment epithelium (RPE) or neurosensory retina cells." Specification paragraph 20. Those of ordinary skill in the art understand that within this context, the inner segment of the eyeball is the interior tissue of the eye comprising retinal cells, and particularly the retinal pigment epithelium (RPE). Thus, Applicants respectfully request that the rejection be withdrawn.

Further, claims 11 and 12 are rejected as allegedly being indefinite with regard to the recitation of gene "expression." Applicants respectfully disagree. Because tissue specific (or preferential) expression is a well known term of art, those of ordinary skill would know the metes and bounds of the term. It is unnecessary to provide a "reference cell or tissue" where the general art provides guidance in determining when a gene is differentially expressed. As such, Applicants respectfully request that the rejection be withdrawn.

In addition, claim 20 is rejected as allegedly being indefinite with regard to the recitation of expression of dsRNA from vector. Applicants have amended the claim to depend from claim 20 as suggested by the Examiner, thus obviating the rejection.

Finally, claim 26 is rejected as being indefinite with regard to the term relating to the form of administration. The claim has been amended to recite the form of administration, thereby obviating the rejection.

Claims 2, 7, 13, 21-22, 24-28, 31, and 54 are rejected under 35 USC § 102, in light of Carter (U.S. Patent No. 5,712,257). Applicants note that the claims are now amended to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. Carter fails to teach how to deliver dsRNA across the blood-brain or the blood-retina barrier. Moreover, there is no indication that dsRNA can even cross the blood-brain or the blood-retina barrier. The additional references to other elements of the claims merely recite added elements, without addressing this primary deficiency. As such, Carter does not teach or even suggest each and every element of the claims. Thus, withdrawal of the rejection is respectfully requested.

Claims 2-3, 5-10, 13, 19-22, 24-28, 31, 46, and 50-54 are rejected under 35 USC § 102(a) and 35 USC § 102(e), in light of LeFleur et al. (U.S. Patent No. 6,433,145). Applicants note that the claims are now amended to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. LeFleur et al. fails to teach how to deliver dsRNA across the blood-brain or the blood-retina barrier. Moreover, there is no indication that dsRNA can even cross the blood-brain or the blood-retina barrier. The additional references to other elements of the claims merely recite added elements, without addressing this primary deficiency. As such, LeFleur et al. does not teach or even suggest each and every element of the claims. Thus, withdrawal of the rejection is respectfully requested.

Claims 2-13, 21-22, 24-28, 31, 46, 50, and 54 are rejected under 35 USC § 102(a) and 35 USC § 102(e), in light of King (U.S. Patent Application No. 2002/0165158). Applicants note that the claims are now amended to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. King fails to teach how to deliver dsRNA across the blood-brain or the blood-retina barrier. Moreover, there is no indication that dsRNA can even cross the blood-brain or the blood-retina barrier. The additional references to other elements of the claims merely recite added elements, without addressing this primary deficiency. As such,

King does not teach or even suggest each and every element of the claims. Thus, withdrawal of the rejection is respectfully requested.

Claims 2, 5-10, 13, 19-22, 24-28, 31, and 48-54 are rejected under 35 USC § 102(e), in light of Tolentino et al. (U.S. Patent No. 7,148,342). Applicants note that the claims are now amended to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. Tolentino et al. fails to teach how to deliver dsRNA across the blood-brain or the blood-retina barrier. Moreover, there is no indication that dsRNA can even cross the blood-brain or the blood-retina barrier. The additional references to other elements of the claims merely recite added elements, without addressing this primary deficiency. As such, Tolentino et al. does not teach or even suggest each and every element of the claims. Thus, withdrawal of the rejection is respectfully requested.

Claims 2-13, 19-22, 24-28, 31, 46, and 48-54 are rejected under 35 USC § 103, in light of Robinson et al. (U.S. Patent No. 5,814,620) in view of LeFleur et al. (U.S. Patent No. 6,433,145), and Tuschl et al. (U.S. Patent Application No. 2002/0086356). Applicants note that the claims are now amended to recite a method for delivery of oligoribonucleotides across the blood-brain or the blood-retina barrier. The references when viewed in combination all fail to teach how to deliver dsRNA across the blood-brain or the blood-retina barrier. Moreover, there is no indication that dsRNA can even cross the blood-brain or the blood-retina barrier. The additional references to other elements of the claims merely recite added elements, without addressing this primary deficiency. As such, the reference do not teach or even suggest each and every element of the claims. Thus, withdrawal of the rejection is respectfully requested.

Claims 2, 5-13, 21-22, 25-28, 31, 48, and 50-54 are rejected under the judicially created doctrine of obviousness type-double patenting in light of U.S. Patent Application Publication No. 2006/0003915). Applicants submit a timely filed terminal disclaimer herewith, thereby obviating the rejection.

CONCLUSION

For at least the reasons discussed above, Applicant respectfully requests reconsideration of the rejections of the claims. Applicant believes that these claims define over the prior art of record and are in proper form for allowance. If the undersigned can be of assistance to the Examiner regarding any of the above, please contact the undersigned at the number set forth below.

It is not believed that any additional fees are due; however, in the event that an additional fee is required for this response, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-0436.

Respectfully submitted,

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